

### **Remarks**

After entry of this Amendment, claims 106, 112-115, 118, 120-124, and 129-138, as amended, will be pending for the Examiner's review and consideration. Claims 107-111, 116, 117, 119, and 125-128 have been canceled without prejudice. The right to prosecute the subject matter of any of the canceled claims in this or in a subsequent continuation, continuation-in-part, or divisional application is hereby expressly reserved.

### **Claim Amendments:**

Claims 106 and 124 have been amended to recite a vesicular composition "consisting essentially of" the recited components. Claims 106 and 124 have also been amended to replace "aqueous medium" with "buffer." This amendment is supported, for example, on page 24, lines 6-13, and page 37, lines 8-10, of the Specification as filed. No new matter has been added to the claims by these amendments.

### **Claim Rejections – 35 U.S.C. § 112:**

Claims 106-110, 112-118, and 120-138 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. This rejection has been rendered moot as to claims 107-110, 116, 117, and 125-128 by their cancellation without prejudice. As to the remaining claims, this rejection is respectfully traversed.

Claims 106, 112-115, 118, and 120-123 recite a vesicle consisting essentially of: i) one or more phosphatidyl cholines; ii) a salt of one or more non-steroidal anti-inflammatory drugs ("NSAIDs"); and iii) one or more antioxidants. Claims 124 and 129-138 recite vesicles consisting essentially of: i) one or more phosphatidyl cholines; ii) a salt of one or more NSAIDs; iii) one or more antioxidants; and iv) one or more consistency modifiers and/or one or more stabilizers.

The Office asserts that the specification does not describe a vesicle "consisting essentially of" a phosphatidylcholine and a salt of an NSAID.

It is respectfully submitted that Examples 18-25 disclose vesicles consisting essentially of, *inter alia*, a sodium salt of ibuprofen, rather than ibuprofen (acid form) as

the Office asserts. Examples 18-25 state: "The preparation is as described in Examples 1 to 4, with the exception that, after the mixture is suspended, the pH is adjusted to a value of 7 by the addition of 10 M NaOH." (Specification, p. 37, lines 8-10 (emphasis added)). The addition of NaOH converts the ibuprofen (acid form) into its sodium salt. Accordingly, Examples 18-25 describe vesicles consisting essentially of, *inter alia*, containing ibuprofen sodium salt.

For these reasons, it is believed that the claims find written description support in the specification as filed, and that this ground of rejection should be withdrawn.

Claim Rejections – 35 U.S.C. § 103(a):

Claims 106-110, 112-118, and 120-138 stand rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Vyas, et al., *J. Microencapsulation*, 1995, 12(2), 149-154 ("Vyas"); U.S. patent No. 5,585,109 to Hayward, et al. ("Hayward"); or U.S. patent No. 4,937,254 to Sheffield, et al. ("Sheffield") in combination with U.S. patent No. 5,043,165 to Radhakrishnan ("Radhakrishnan") or U.S. patent No. 5,498,420 to Edgar, et al. ("Edgar"), by themselves or together in further combination with U.S. patent No. 4,897,269 to Mezei ("Mezei"). These rejections have been rendered moot as to claims 107-110, 116, 117, and 125-128 by their cancellation without prejudice. As to the remaining claims, these rejections are respectfully traversed for the reasons set forth below.

*Vyas alone or in combination with Radhakrishnan, Edgar and/or Mezei:*

Vyas does not disclose or suggest the recited vesicular compositions of present claims 106, 112-115, 118, 120-124, and 129-138.

In particular, Vyas does not disclose or suggest either the recited at least one antioxidants or the recited vesicle that is capable of penetrating through a permeability barrier having at least one constriction, wherein the vesicle is larger than the constriction by more than a factor of 2 and less than a factor of 4.

In addition, Vyas does not teach or suggest the recited vesicular compositions consisting essentially of a vesicle and a buffer. In stark contrast, Vyas's compositions comprise an *oil-in-water emulsion*, rather than a buffer solution. (Vyas, p. 150,

penultimate paragraph). Further, Vyas does not provide any expectation whatsoever that replacing its oil-in-water emulsion with a buffer recited in the present claims would have successfully provided vesicles capable of transporting an NSAID through intact human or animal skin or mucous membranes and penetrating through a permeability barrier having at least one constriction, and the vesicle is larger than the constriction by more than a factor of 2 and less than a factor of 4. Indeed, the Federal Circuit has recently held that identifying a reasonable expectation of success is crucial in “unpredictable” arts, such as chemistry, because “[t]o the extent an art is unpredictable, as the chemical arts often are . . . potential solutions are less likely to be genuinely predictable.” *Eisai Co. Ltd. v. Dr. Reddy’s Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008).

None of the secondary references cited by the Office, either alone or in combination, remedies the above-described deficiencies of Vyas.

*Hayward alone or in combination with Radhakrishnan, Edgar and/or Mezei:*

Hayward does not disclose or suggest the recited vesicular compositions of present claims 106, 112-115, 118, 120-124, and 129-138.

Further, the transitional phrase “consisting essentially of,” as it relates to the vesicles of the present claims, excludes from the vesicles non-steroidal anti-inflammatory drugs that are not in salt form. Claims 108-110 and 126-128 have been canceled without prejudice.

As previously argued, Hayward discloses “liposomal dispersions containing ***un-neutralized*** salicylic acid.” Hayward, col. 1, lines 13-15 (emphasis added). Accordingly, Hayward teaches away from using a salt of one or more NSAIDs by emphasizing the importance of using salicylic acid (acid form) as compared with neutralized salicylic acid (*i.e.*, salicylic acid in salt form).

None of the secondary references cited by the Office, either alone or in combination, remedies the above-described deficiency of Hayward because none of Radhakrishnan, Edgar, and Mezei discloses a vesicle having the recited salt of one or more NSAIDs.

Sheffield alone or in combination with Radhakrishnan, Edgar and/or Mezei:

Sheffield does not disclose or suggest the recited vesicular compositions of present claims 106, 112-115, 118, 120-124, and 129-138.

In particular, Sheffield at least does not disclose or suggest administration of a vesicle to human or animal skin that is intact. Rather, Sheffield teaches away from such administration by emphasizing the delivery of its disclosed liposomes to a “site of surgical trauma” on the skin (*i.e.*, portions of the skin that have been injured, for example, by incision). Sheffield, col. 3, ll. 39-56, ll. 15-17, 42-44.

None of the secondary references cited by the Office, either alone or in combination, can remedy the above-described deficiency of Sheffield because none of Radhakrishnan, Edgar, and Mezei discloses a method for transporting an NSAID salt through intact human or animal skin or mucous membranes, comprising administering to the skin or a mucous membrane of a human or an animal a vesicular composition consisting essentially of a vesicle that consists essentially of: i) one or more phosphatidylcholines; ii) a salt of one or more non-steroidal anti-inflammatory drugs (“NSAIDs”); and iii) one or more antioxidants (claims 106, 112-115, 118, and 120-123); or i) one or more phosphatidylcholines; ii) a salt of one or more NSAIDs; iii) one or more antioxidants; and iv) one or more consistency modifiers and/or one or more stabilizers (claims 124 and 129-138), and that is capable of penetrating through a permeability barrier having at least one constriction, wherein the vesicle is larger than the constriction by more than a factor of 2 and less than a factor of 4.

Because none of the primary references Vyas, Hayward, or Sheffield, either alone or in combination with Radhakrishnan or Edgar by themselves or in further combination with Mezei discloses or suggests all of the recitations of present claims 106, 112-115, 118, 120-124, and 129-138, it is believed that the Office has failed to make out a *prima facie* case of obviousness of these claims. Accordingly, the rejections of these claims under 35 U.S.C. § 103(a) as obvious over Vyas, Hayward, or Sheffield in view of Radhakrishnan or Edgar, by themselves or in further combination with Mezei cannot stand and should be withdrawn by the Office.

Conclusion:

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the Examiner is invited to contact the undersigned at (212) 497-7731 to discuss the same.

No fee is believed to be due for the submission of this response. Should any fees be required, please charge all such fees to Wilson, Sonsini, Goodrich & Rosati Deposit Account No. 23-2415 (Docket No. 35946-701.831).

Respectfully submitted,

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